


PAPER

Preserving fertility in women with cancer (PreFer): Decision-making and patient-reported outcomes in women offered egg and embryo freezing prior to cancer treatment

Katharina S. Vogt¹  | Jane Hughes¹ | Anna Wilkinson² | Neda Mahmoodi¹ | Jonathan Skull³ | Hilary Wood⁴ | Sophia McDougall² | Pauline Slade⁵ | Diana M. Greenfield⁶ | Allan Pacey⁷ | William Ledger⁸ | Georgina L. Jones¹

¹Department of Psychology, School of Social Sciences, Leeds Beckett University, Leeds, UK

²Medical School, University of Sheffield, Sheffield, UK

³Reproductive Medicine and Surgery, Assisted Conception, Jessop Wing, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

⁴School of Health and Related Research, University of Sheffield, Sheffield, UK

⁵Institute of Psychology Health and Society, University of Liverpool, Liverpool, UK

⁶Late Effects, Sheffield Teaching Hospitals NHS Trust and Honorary Professor, Department of Oncology and Metabolism, University of Sheffield. Weston Park Hospital, Sheffield, UK

⁷Academic Unit of Reproductive and Developmental Medicine, Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK

⁸University of New South Wales, Sydney, NSW, Australia

Correspondence

Katharina S. Vogt, Research Associate, Department of Psychology, School of Social Sciences, Leeds Beckett University, Leeds LS1 3HE, UK.

Email: k.s.vogt@leedsbeckett.ac.uk

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Abstract

Objective: Women of childbearing age with new cancer diagnoses have to make rapid decisions about fertility preservation (FP) before starting cancer treatment (CT). The aim of the PreFer study was to explore this FP decision-making process and its impact on patient-reported outcomes (PROMs) and health-related quality of life (HRQoL).

Methods: A prospective, mixed-methods design was used (questionnaires, in-depth interviews). Interviews were analysed using thematic analysis. Fifty-eight women with new cancer diagnoses were recruited. Comparisons were made between women who declined FP referral in oncology (Group1) and women who chose referral (Group2). Group 2 was further split into those who had some FP (2A) and those who did not (2B). Questionnaires and PROMs were administered prior to and after the fertility consultation, before the start of CT and 3 months post CT. Interviews were conducted with one participant from Group 2.

Results: HRQoL was negatively affected, particularly depression. Women's lack of understanding about the relationship between CT and fertility were evident. Five themes emerged from the interviews as barriers and facilitators to the FP decision-making process.

Conclusion: The results indicate that better information and support resources aimed at women to support their decision making are needed, such as patient decision-aids. Women from Group 1 were found to suffer significantly worse depression compared with the general UK population, highlighting the need for psychological support in the FP care-pathway and for research exploring the contributions of depression and hopelessness to the decision-making process.

KEYWORDS

females, fertility preservation, mixed methods, prospective study, reproductive age

1 | BACKGROUND

One in two people born after 1960 will be diagnosed with cancer during their lifetime.¹ With survival rates having doubled in the UK in the last 40 years,² the late effects of cancer and its treatment on long-term quality of life issues, such as fertility and future childbearing, must be considered.

A permanent loss of fertility can be a side-effect of cancer treatments (CTs), and it is estimated that 40% to 70% of female cancer patients of reproductive age will experience impaired fertility afterwards^{3,4}; fertility loss therefore epitomises one of the most significant and distressing late-effects.^{5,6} Fertility preservation (FP) treatments before starting CT give patients the opportunity to have future, biological offspring. To enable women to make informed decisions about this, professional and regulatory bodies recommend that FP options are discussed during the initial stages of treatment.^{7,8}

A range of FP treatments are available for female cancer patients (embryo cryopreservation, oocyte cryopreservation, and ovarian tissue cryopreservation amongst others^{9,10}). Decisions about FP have to be made rapidly and before the start of CT; they are often stressful, complex, and eternally binding. Simultaneously, they require co-ordination of services beyond the oncology department.

Despite professional guidelines, there are operational problems in the FP care pathway for patients with cancer in the NHS.¹¹ For example, although the Department of Health emphasises “no decision about me, without me”,⁹ current practice does not reflect this, indicated by the population's low referral to fertility services and treatment rates.^{10,12} Many female cancer patients are either not referred or do not feel well supported in making FP decisions¹³: one study reports that only 12% of 170 women with breast cancer were referred for FP, with many unaware that infertility could be a consequence following chemotherapy.¹² A recent narrative review examining the barriers to the decision-making process for women with cancer contemplating FP treatment,¹¹ identified six key themes (lack of fertility information provision; non-referral to FP-services; fear concerning the perceived risks of delaying CT; decisions around prioritising one treatment over another; personal situation, and the cost of FP treatment). This review highlights factors, from the patient and health care professional perspectives, acting as barriers to the FP decision-making process. The review also found most studies conducted in this area were retrospective qualitative studies with no explorations of quantitative outcomes, such as patient-reported health-related quality of life (HRQoL) or psychological wellbeing measures.

Therefore, the PreFer study applied a prospective design and sought to (1) investigate factors influencing the decisions women with new diagnoses of cancer make about their fertility, and (2) compare the quality of life, levels of anxiety, depression, illness perceptions, and optimism between women who chose to preserve their fertility and those who do not.

2 | MATERIALS AND METHODS

NHS ethical approval was granted (Reference: 11/YH/0043) for this exploratory and pragmatic mixed-methods study. It was the aim to

recruit the maximum number of participants in this single, tertiary referral centre during 18 months.

2.1 | Participants

Women (16-40 years), with a new diagnosis of cancer and planned potentially gonadotoxic treatment (chemotherapy and/or radiotherapy), were eligible. Data from two groups of women were collected: Group 1 from Oncology (women with new diagnoses of cancer who chose not to be referred to the Assisted Conception Unit [ACU]) and Group 2 recruited from the ACU (who chose to see the fertility expert). Group 2 was subsequently divided into women who made a positive FP decision (Group 2A), and those who did not (Group 2B). Group 1 acted as a comparison for Group 2.

2.2 | Procedure and measures

Supplementary File 1 illustrates overall patient flow through the study.

Group 1: A member of the oncology care team gave the patients the information sheet, the Hospital Anxiety and Depression Scale (HADS) and a short study-specific decision-making questionnaire (Supplementary File 2). The study-specific questionnaire ascertained levels of understanding of the impact of CT on fertility and knowledge of FP treatments. The HADS detects the presence and severity of degrees of mood disorder, anxiety, and depression.¹⁴ Scores for each HADS subscale (anxiety, depression) range from 0 to 21; categorised as normal (0-7), mild (8-10), moderate (11-14) and severe (15-21). Overall HADS scores indicate levels of emotional distress scale (0-42). Consent was deemed given when completed questionnaires were returned. No further data was collected for Group 1.

Group 2: Questionnaires were administered at five time points during the care pathway to measure aspects of decision-making, patient satisfaction and HRQoL. Before the initial ACU consultation (baseline), the study specific decision-making questionnaire (like Group 1, Supplementary File 2), the HADS, the European Organisation for Research on Treatment of Cancer QLQ C30 (EORTC-QLQ-30), the Life Orientation Revised questionnaire (LOT-R), and Brief Illness Perceptions Questionnaire (BIPQ) were administered. The EORTC-QLQ-30 measures HRQoL.¹⁵ The 10-item LOT-R was used to measure optimism and pessimism.^{16,17} The women's cognitive and emotional representations of their cancer were assessed using the brief version of the Illness Perception Questionnaire (BIPQ).¹⁸ Immediately following this initial FP consultation (Time 1a), the shorter 24-item version of The Princess Margaret Hospital Satisfaction with Doctor Questionnaire¹⁹ was administered, measuring patient's satisfaction with their doctor (two domains: doctor disengagement, perceived support).

A second set of study-specific questions were administered before the start of superovulation treatment (Time 1b; Supplementary File 3) with questions investigating (1) the reasons for FP choice, (2) changes in the women's level of understanding of the impact of CT

on their fertility, and (3) knowledge of FP options following their initial consultation. Despite negative decisions, Group 2B also received a second set of questions prior to the start of CT exploring reasons for not wishing to undergo FP (Time 1b).

Prior to CT, women in Group 2 (A + B) completed the HADS and EORTC-QLQ 30. All four questionnaires were completed again (EORTC-QLQ-30, HADS, IPQ, and LOT-R) 3-months post CT (Time 3).

Demographic data (eg, age, relationship status) and clinical data (eg, diagnosis-related, treatment details, stage of disease) were recorded at entry and updated sequentially.

2.2.1 | Qualitative study

All women in Group 2 (A + B) were invited for semi-structured interviews to explore their experiences of the FP process. Sampling was assumed complete when theoretical saturation was reached.

Interview schedules were semi-structured. Interviews were recorded, transcribed, and coded using the QSR NVivo 9 Qualitative Data Analysis Software. Interviews were anonymised. Participants were invited by telephone, after having already received information in the initial patient information sheet. If interested, the women were asked to attend an hour earlier for their appointments or at another convenient time. Written consent was obtained.

2.3 | Analysis

Statistical analyses were carried out using SPSSv23. Summary statistics were used to describe the mean scores of Group 2 overall, then by groups 2A and 2B to explore differences (independent t-tests, ANOVAs). A repeated-measures ANOVA (with Bonferroni post-hoc comparisons) was used to explore differences over time (3 time points) for the HADS and EORTC.

Qualitative analysis utilised thematic analysis, utilising a five-step approach (Familiarisation, Generation of Initial codes, Searching for Themes, Reviewing Themes, Defining and Naming Themes).²⁰ Interviews were collaboratively analysed and emergent themes discussed to reach consensus (G.J., H.W., J.H.). Qualitative analysis was undertaken using NVivo 11.

3 | RESULTS

Group 1:

Group 1 consisted of 34 women; their mean age was 34 (SD = 4.8; 23-40). The majority had breast cancer ($n = 21$), followed by cervical cancer ($n = 7$); other diagnoses were lymphoma ($n = 2$), leukaemia ($n = 2$), and rectal cancer ($n = 2$).

3.1 | Reasons for non-referral to ACU

Reasons for non-referral are illustrated in Supplementary Table 2. Most commonly, referral was declined due to having completed their family and not wanting more children ($n = 13$). Four women had already had children and felt they were too old for more; these women were typically in their late 30ies/early 40ies. Four women stated they never wanted children. Six women stated that CT was priority. Two

women had already had children but declined due to worries about cancer re-occurrence and its potential effect on family members. Other reasons included having an oestrogen positive cancer ($n = 1$), not being offered referral ($n = 1$), financial reasons ($n = 1$), and already having endured too much physical stress ($n = 1$); (missing $n = 1$). Many women gave answers indicating multiple factors impacting their decision. One woman, aged 27, said fertility was not a priority for her at the moment and that she may revisit her wish for future children after treatment.

The analysis of HADS scores for anxiety revealed that women were more anxious (mean = 7.32; median = 8.0; range 0-13) compared with the normative HADS data (mean = 6.96; median = 6.0). For depression, it was revealed that women in Group 1 were also significantly more depressed (mean = 6.73; median = 7.0, range = 1-13) compared with the normative mean of 3.92 and a median of 3.²¹

Additionally, women felt their chances of having a baby following CT was 1.71 using a visual analogue scale on a scale of 0 to 10 (0 = no chance and 100 = excellent chance). They also felt their chances of having children compared with any other woman with cancer was about 40% (4.07).

Group 2:

Supplementary Table 1 illustrates the demographic details of Group 2 (2A+ 2B), consisting of 23 women with a mean age was 29.2 years (SD = 6.3, range: 16-39). All but one participant (African-American, ID-number:15, Supplementary Table 1) were White British. The majority had breast cancer ($n = 14$, 61%), four ($n = 4$, 17.4%) lymphoma and five were diagnosed with other cancers (Sarcoma, cervical, rectal, brain, and tonsils; $n = 5$, 21.5%). Thirteen had partners.

Two women died while taking part in the study. Two women subsequently died; another became pregnant naturally. Complete T1, T2, and T3 data on 20 women was available (of whom 14 women across groups 2A and 2B were interviewed). No treatment was delayed because of FP.

Before the consultation with the fertility expert (baseline), nearly half of the women (43.5%) did not know or were not sure to what degree CT may affect their fertility. Seventeen percent thought their fertility would be moderately affected, and 39% thought this would be a lot. When the 23 women were asked if they were aware of options available to women to preserve fertility before undergoing CT, 87% were aware of freezing embryos and 95.7% were aware of freezing eggs.

After initial consultation with the fertility expert, four women decided not to pursue any any FP (3, 20, 22, 24). Reasons included "fear of spreading and aggressiveness of the cancer," not being able to face "the amount of procedures with so little chance at the end," and having a poor prognosis.

Fifteen women made a FP decision after meeting with the ACU expert (1, 4, 5, 6, 7, 9, 10, 11, 12, 13, 17, 18, 19, 21, 23). Four chose egg freezing (4, 7, 12, 13); eight chose embryo freezing (1, 5, 6, 9, 11, 17, 18, 21) and three chose to freeze both (10, 19, 23). All eight participants who chose embryo over egg freezing stated that it was because they thought it either the best option or most likely to succeed. Two of the four, who initially opted for egg freezing, stated

not having partners as their main reason and two felt it was their best option for example being "due to start chemotherapy," and having "more chance of conceiving by egg freezing than egg freezing and embryo."

In the end, 12 women (52.2%) underwent FP treatment, three froze eggs only (4, 7, 12), six froze embryos (1, 5, 6, 9, 18, 21) and three froze both eggs and embryos (10, 19, 23). Eleven of these women received NHS funding for their treatment and one self-funded (5).

The remaining 11 of the 23 women (47.8%) did not undergo any FP treatment. Four declined immediately ($n = 4$); further reasons included not receiving NHS funding ($n = 3$), having an oestrogen positive cancer ($n = 1$), and being too ill ($n = 1$). One withdrew prior to treatment as she felt too overwhelmed, and the reasons for one woman not to undergo FP are unknown.

Six women were still undecided. Reasons for uncertainty included financial costs, "too big a decision to make" and "a lot of information to take in." One needed to discuss fertility with her oncologist while another needed to talk to her partner/family.

In response to the question: "Is there anything else that would have made you decide differently?" the six undecided women gave a variety of reasons, including "If I had a guarantee of how IVF treatment can affect my oestrogen receptor +ve cancer"; "maybe if I had a partner I would have had embryo freezing."

In comparison, 10 out of the 12 women who underwent FP answered stated there was nothing else that would have made them decide differently after their initial consultation with the fertility expert.

3.2 | Patient satisfaction with the fertility consultation

PMH-PSQ scores revealed patients felt very well supported by their fertility doctor (mean = 44, range 30-57) feeling low disengagement during the consultation (mean = 17.2, range 13-35). Interestingly, using a visual analogue scale on a scale of 0 to 10 (0 = no chance and 100 = excellent chance), women felt their chances of having a baby following CT had significantly improved following the consultation. At baseline women felt their chances would be 4.0, rising to 5.1 ($P = 0.033$). However, they still always felt their chances of having children were significantly worse than any other woman with cancer before seeing the fertility expert (4.3 vs 6.2, $P = 0.001$).

3.2.1 | Analysis of other questionnaire scores

Questionnaire scores for the HADS, EORTC, and LOT-R across each time point were calculated for all Group 2.

No statistically significant differences between baseline and time 3 (3-months post CT) were observed in the scores for the whole group. However, one significant difference was observed between the scores from baseline to time 3 for the women overall, as measured on the BIPQ. Women felt they experienced significantly ($P = 0.010$) more symptoms at time-3 compared with baseline.

A comparison of baseline-HADS scores between Group 1 and Group 2 (ie, before seeing the fertility expert) revealed no significant differences ($P > 0.05$). However, median HADS depression and anxiety scores were worse for women who chose not to preserve their fertility compared with those who did. Group 1 had a median anxiety score of

8, and 7 for depression. Group 2 had a median value of 6 for anxiety, and 5 for depression.

When comparing subgroup scores by those who chose to preserve their fertility (2A) and those that did not (2B), an analysis of the data over time again revealed no significant differences on the LOT-R.

When comparing the mean scores on the visual analogue scale, women in Group 1 felt they had significantly less chance of getting pregnant after CT compared with Group 2 ($P < 0.001$). There was no significant difference between women in group 1 and 2 in terms of how they perceived their chances of having a baby following CT, compared with other women ($P > 0.05$).

In relation to the EORTC, physical functioning appeared to significantly worsen over time for women who chose not to preserve their fertility ($F(2, 14) = 4.68$, $P = 0.028$), but this did not remain following Bonferroni post-hoc comparisons ($P > 0.05$). While there were no significant differences over time in relation to Role functioning, Bonferroni post-hoc comparisons revealed that the role functioning of women who chose to preserve their fertility was significantly better at time 3 compared with baseline ($P = 0.049$) a pattern not demonstrated in 2B.

HADS comparison between Group 1 and 2

A comparison of HADS scores between Group 1 and Group 2 before they had seen the fertility expert revealed no significant differences ($P > 0.05$). However, it is important to note that median depression scores (7.0) and anxiety scores (8.0) were worse for group 1 than group 2 overall (5, 6, respectively).

Comparing the mean scores on the visual analogue scale women in Group 1 felt they had significantly less chance of getting pregnant after CT, compared with the women in group 2 ($P < 0.001$). There was no significant difference between women in group 1 and 2 in terms of how they perceived their chances of having a baby following CT, compared with other women ($P > 0.05$).

3.2.2 | Qualitative results

Fourteen women were interviewed (aged 16-39, mean: 31). Eleven had breast cancer; three had other cancers (rectal cancer, lymphoma). One breast cancer patient had a further diagnosis of metastatic cancer but wanted to take part in the interview. The youngest participant was 16 and the oldest 39. Of the women interviewed, half underwent some form of FP treatment. Three declined FP initially, and one initially decided to proceed but withdrew before undergoing the FP procedures. Three women did not proceed due to lack of NHS funding. Four women froze embryos only, one woman froze eggs only, and two women froze both eggs and embryos. Transcripts were analysed collectively regardless of FP decision,

3.2.3 | Emergent themes

Five overarching themes were identified; data within each theme were divided into promoters and facilitators (Supplementary Table 3) to FP referral and/or treatment. The themes were 1) Timing and quality of information provision; 2) Psychosocial factors; 3) Age; 4) Clinical Influences; and 5) Financial cost.

1) Timing and quality of information provision

The main theme emerging from the interviews was that women wanted more information about their FP options, regardless of cancer diagnosis. Many wanted written information to take away and digest, as well as verbal discussions with their oncologist/surgeon/specialist cancer nurse. Many also described a process of searching for relevant information, for example from sources such as the internet, friends and families, and charity publications.

The timing of when information is shared with the women was also key: women reported receiving extensive information at their fertility consultation, but wanting to receive this information earlier in their care pathway to enable them to start thinking about FP options and about questions to ask the fertility consultant.

Most participants expressed a desire for more information from their oncologist or surgeon, particularly in relation to risk statistics, effect of different chemotherapy regimens, and whether a delay would increase risk. One participant described a process of trying to weigh up her options but needing more information on what delaying CT might mean.

2) Psychosocial factors

Fear was a dominant emotion expressed by many women, both in terms of the cancer itself and future health outcomes; as well as the associated fear of delaying chemotherapy for FP. Many also outlined a process of balancing risk of delaying treatment in the context of fear of exacerbating their cancer, or increasing the possibility of a recurrence against the desire for a future child. Other concerns related to having hormone-sensitive breast cancer. Anxieties about what the actual fertility process would involve was a barrier to two women in the study. Women were also concerned about passing a genetic cancer risk to any future children.

3) Age

Age appears to be a significant factor in the decision of FP, acting as both barrier and promoter. Older women frequently stated they had chosen not to consider FP often due to concerns about the age they would be once they had finished their CT, particularly if a long course of tamoxifen was prescribed. Conversely, older age at diagnosis was seen as a reason to preserve existing fertility. Younger age was stated as a reason not to preserve fertility by one 16-year-old lymphoma patient but stated as a reason for preserving fertility by 29-year-old patient. Relationship status was a potential barrier to two single women in the study.

4) Clinical influences

Women were overwhelmingly positive about support and care received from health care professionals (consultants, nurse specialists and clinical support staff); they commented they were happy with the oncology and surgical teams, their speed and thoroughness—despite some issues around the timing of information provision. Women saw the opportunity to consider FP as positive, describing

“peace of mind,” being able to “turn the negative of cancer into a positive” and giving “hope.” One patient, despite being ineligible for funding, still described the opportunity to have the fertility consultation as positive. Some women specifically expressed concern over the actual preservation process. Many were concerned about how painful or uncomfortable the process might be; one felt “apprehensive.” All reflected that it was less painful and uncomfortable than expected.

5) Financial cost

For some women, financial cost of fertility treatment meant they were unable to go ahead with FP, resulting in disappointment and sadness. One woman said she had not cried at her diagnosis but cried when she discovered she would have to pay for fertility treatment and could not afford this.

Several women who found out they were not eligible for NHS funding reported the financial cost of fertility treatment to be a major barrier for them. Women felt strongly that the potential cost of FP should be disclosed by oncologists at the point of referral to the ACU. Three women expressed disappointment at having their “hopes raised” at being referred to fertility services, only to discover that they were ineligible for funding. Women also expressed an emotional impact on their partners (sadness, anger) about not being able to access FP due to financial cost.

For women who could pay for their fertility treatment, or were able to successfully obtain NHS funding, financial costs were not such an issue. Women expressed relief at being able to go ahead with treatment.

4 | DISCUSSION

The main aims of this study were to (1) investigate the factors that influence decisions women make about their fertility, and (2) to compare the quality of life and levels of anxiety, depression, illness perceptions, and optimism between the women who have decided to opt and not opt for oocyte or embryo freezing.

Recently, a large study has been undertaken to generate UK normative data for the HADS, in which median values have been reported.²¹ The mean ages of the groups in the current study were 34 (Group 1) and 29.2 (Group 2). Using the normative scores for 30 to 34-year-old females, the median normative data for depression are 3; and 6 for anxiety.²¹ These numbers also concur with findings obtained by a non-clinical broadly representative UK adult sample (not adjusted for age or gender).²² The HADS scores in our groups are considerably higher: Group 1 had a median anxiety score of 8, and 7 for depression. Group 2 had a median value of 6 for anxiety, and 5 for depression. In terms of anxiety, the groups scored average (Group 2) or higher-than-average (Group 2); and both groups scored significantly higher on the depression scores in comparison to the UK general population, especially Group 1.

This is an important novel finding, and the presence of depression in female cancer patients as well as its impact on FP decisions requires discussion. In our qualitative findings, hope was a key facilitator for undergoing FP; feeling hopeless may therefore act as a barrier to

undergoing FP and could be a direct consequence of feeling depressed. The finding that women in Group 1 had significantly less belief that they would get pregnant post-CT than women in Group 2 (before first ACU appointment) might reflect this. Furthermore, this may mean that women, who have more hope, are more likely to take the FP referral.

However, barriers of depression or hopelessness cannot be the only reason for women not to take up ACU referrals in oncology. For example, more women in Group 1 had leukaemia and may therefore have been less well and required more immediate treatment compared with women with other cancers. Declining the referral seemed an easy decision for women who considered their family complete or who never wanted children. However, for a small number of women, reasons for declining FP in oncology did not appear evidence based—such as, feeling too old, or reporting that the fertility discussion had not taken place. This finding concurs with past research suggesting judgements made by oncologist, bases upon the individual characteristics of patients, were acting as barriers for FP referral.^{14,23}

Findings from those women, who chose to have FP consultations, support the evidence that the decision-making process is emotional, complicated, and individual to each patient (eg,^{7,14}). Individuality of the decision-making process is, for example, illustrated in the finding that age was cited as both a reason for and against FP treatment.

Women's age at completion of CT, for example, was noted to be a factor in the decision not to proceed with FP, as many women felt they would be too old to become pregnant after 5 years of extra treatment. However, while it is not advised that women become pregnant whilst taking Tamoxifen, there are some cases of women taking a "Tamoxifen vacation"; interrupting medication to become pregnant, then returning to it having had a baby. Huang et al²⁴ describe a woman who was considering to do so, but her husband and physician did not recommend it. However, currently there is little evidence suggesting a "Tamoxifen vacation" could be harmful, although due to the half-life of the drug and its potentially teratogenic effects, postponing pregnancy for 3 months after cessation of Tamoxifen therapy is recommended. A clinical trial is currently being conducted to investigate this.²⁵

Additionally, cancer type may also act as barriers to positive FP decision: Firstly, different age groups are most at risk of different cancer types. While breast cancer (BC) is the most common cancer for women of reproductive age, young women typically suffer more aggressive forms of BC requiring urgent treatment. For teenagers and young adults (aged 15–24), carcinomas and lymphomas are most common, also often requiring immediate treatment.²⁶ While chances of fertility returning after CT are usually greater in younger patients, the types of cancer diagnosed in younger women may require more aggressive or immediate treatments, causing greater damage to fertility or not allowing time for FP.

Secondly, having an oestrogen receptor positive (ER+ve) cancer type was a barrier for ACU referral or positive FP decision for three women with BC. Around 80% of breast cancers are ER+, and 65% of these cancers are also progesterone receptor positive (PR+ve).²⁷ Despite lack of evidence for any negative effect on the cancer, medical professionals are reluctant to refer ER+ve patients to ACUs due to the stimulation of the ovaries involved in FP.^{23,28}

Timing and quality of information provision were further key factors for the FP decision. The majority of patients sought additional information on the internet prior to their FP consultation. Timing of information provision in the case of cancer patients is difficult with many report difficulty processing extra information at the time of diagnosis, several in this study. Despite the difficulty, our patients acknowledged that it would be helpful if given written information for reference. These findings concur with those from an Australian study, who found that women wanted as much information as possible around the time of diagnosis, and that low levels of FP knowledge were associated with greater decisional conflict.²⁹

Despite international guidelines recommending providing FP information at the earliest opportunity,^{7,8,26,30} data from studies of oncologists acknowledge lack of referral and information.^{26,30} One study found that only one third of oncologist surveyed referred patients and routinely provided patients with written information.¹⁰ Similarly, Breast Cancer Care¹² found that more than a third of specialist BC doctors and nurses surveyed did not discuss fertility-related risks of treatment with young female BC patients; 26% additionally stated there was no clear system for directing patients to ACUs. This study, along with others, clearly illustrates that oncology teams need more support and resources to be able to better support fertility decisions.

In our study, one area of inequitable access having the most impact related to funding. Six women did not receive funding, and five were consequently unable to pursue FP. Since completing this study, funding rules have changed in the UK,⁹ but it still may not be available to all, depends very much upon parity and criteria set in place by different clinical commissioning groups. Tackling FP funding for cancer patients should be a priority.

Not all women of reproductive age who undergo treatment for cancer become infertile.⁴ Most women in our study understood this, rating themselves of having a 40% chance of maintaining fertile after CT, before seeing the fertility expert. However, it was encouraging that this had significantly risen to a 50% chance after ACU consultation, along with levels of optimism around having a baby compared with other women with cancer once they had seen the fertility expert. This highlights the importance of the fertility consultation in terms of not only reassuring women about FP but also as a source of support and optimism for these women.

Unfortunately, recent evidence suggests that there is wide variation in access to FP services although some initiatives have recently been launched such as the International Onco-fertility Competency Framework study from Australia in response to the need to improve referral pathways and models of care for cancer and FP services, addressing inequitable access for cancer patients.³¹ With the inherent need for better information resources to be available earlier in the care pathway in oncology, patient decisions aids (PtDAs) may be of value. By definition, they should include all attributes to support decision-making by helping patients to recognise that a decision needs to be made, and being explicit about the risks and consequences involved. Whilst there are many FP resources publicly available for women with cancer, few exist to support the FP decision process in women of reproductive age.³² Although some include two PtDAs designed for women with breast cancer in Australia^{29,33} one in the Netherlands³⁴

and an online version developed in Switzerland³⁵ and a booklet both for women with any cancer which are also currently undergoing development and testing.³⁶

This need for better decisions aids is illustrated by one patient's answer to why she declined a referral to fertility services: "Fertility is not a high priority on my list at the moment, getting through the cancer comes first. Once things settle and if I do wish to have more children then 'thats' when I will go and discuss my options". This clearly demonstrates that the woman either had not had received the correct information or has not understood the implications of her decision not to preserve her fertility.

4.1 | Study limitations

Because of recruitment challenges, sample size was smaller than intended, and this may account for some of the important but non-significant findings that were observed. However, of those recruited, only one withdrew consent with the remaining women supporting the study and data collection. The single centre nature of the study may make findings un-representative of other centres. Although our findings are consistent with those reported in the international literature, it possible that the small sample, especially for Groups 2A and B, is the reason for non-significant results due to a lack of power.

Additionally, it is also possible that other factors were behind the reasons why some women felt they had a lower chance of getting pregnant post cancer treatment (Group 1), such as knowing that aware that FP does not guarantee pregnancy or for practical reasons. This would be interesting to explore in future research.

Furthermore, the qualitative interviews only gave a snapshot of how participants felt on that day, making it difficult to establish changes or experiences over time.

4.2 | Clinical implications

Two conclusions must be drawn as clinical implications. Firstly, women's decisions around their CT and FP are complex and emotional. This study specifically revealed the contribution of depression and hopelessness when declining FP referral or treatment, a novel finding relating to HRQoL. It therefore requires future exploration both in the context of being a barrier to FP in women newly diagnosed with cancer, as well as in the context of psychological interventions aimed at reducing depression to enable women to make decisions irrespective of the presence of depression.

Secondly, more resources designed specifically to support decision-making are needed to support women who felt unable to make decisions, were misinformed by clinicians, or have not received support.

ORCID

Katharina S. Vogt  <http://orcid.org/0000-0003-3911-637X>

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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